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Jean F. Welter

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EXAMINER

BOWERS, NATHAN ANDREW

ART UNIT

PAPER NUMBER

1797

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/578,212	Applicant(s) WELTER ET AL.	
	Examiner NATHAN A. BOWERS	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) 15-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 42-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 1) Claims 1-9, 12, 14, 43 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Vetillard (WO 0206441) – see English language (US 20040132175) for a translation.

With respect to claims 1 and 43, Vetillard discloses a bioreactor comprising a housing (Figure 1:C2) defining a first chamber that contains a first liquid medium. The housing comprises an inlet port (Figure 1:EF2) and an outlet port (Figure 1:SF2) to accommodate a culture medium fluid flow through the first chamber. This is disclosed in paragraphs [0080] and [0096] of US 20040132175. Gas permeable membranes (Figure 1:M1 and Figure 1:M3) define a portion of the housing and allow gas to flow through the housing into the first chamber. Loading modules (Figure 1:C1 and Figure 1:C3) are fully capable of transmitting hydrostatic pressure through the membranes to the first liquid medium contained in the first chamber. Paragraphs [0109], [0134] and [0140]-[0146] indicate that a “downward phase” and an “ascending phase” are created by varying pressures within the loading modules. Furthermore, Vetillard expressly discloses that each inlet and outlet includes a control valve capable of being closed to

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seal any pressure chamber at any time. This is described in paragraphs [0109], [0115] and [0117], and is shown in Figure 6

With respect to claim 2, Vetillard discloses the apparatus in claim 1 wherein the hydrostatic loading module is capable of transmitting pressure by a static second liquid medium. Although Vetillard does not expressly indicate that fluid is retained at a static state within the loading modules before release through the outlet, the device of Vetillard is fully capable of being operated according to this intended use.

With respect to claims 3, 9 and 44, Vetillard discloses the apparatus in claim 1 wherein the hydrostatic modules are attached to the housing and form second and third chambers with the housing. The second and third chambers are separated from the first chamber by gas permeable membranes. This is depicted in Figure 1.

With respect to claims 4 and 5, Vetillard discloses the apparatus in claim 3 wherein the hydrostatic loading modules include pumps (Figure 6:P1 and Figure 6:P3) for increasing and decreasing the pressure of each loading module.

With respect to claim 6, Vetillard discloses the apparatus in claim 4 wherein each loading module comprises an electronic pressure gauge for monitoring pressure in each chamber. This is described in paragraph [0144].

With respect to claims 7 and 8, Vetillard discloses the apparatus in claim 1 wherein the housing comprises a frame that includes a first surface spaced apart from a second surface. The walls of the housing depicted in Figure 1 are considered to represent first and second surfaces. The fluid inlet and fluid outlet are considered to be openings that extend through the frame.

With respect to claim 12, Vetillard discloses the apparatus in claim 1 wherein a pH sensor is provided. This is disclosed in paragraph [0106].

With respect to claim 14, Vetillard discloses the apparatus in claim 1 wherein control valves are provided for regulating fluid flow through inlets and outlets. This is described in paragraphs [0109], [0115] and [0117], and is shown in Figure 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2) Claims 1-14 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vetillard (WO 0206441) as applied to claim 1, and further in view of Jensen (US 20040077075).

With respect to claims 1-9, 12, 14, 43 and 44, Vetillard discloses the apparatus as previously described above. For the sake of argument and in order to expedite prosecution, if Vetillard does not disclose transmitting a hydrostatic pressure and if limitations drawn to the transmission of a hydrostatic pressure do not represent an intended use, then Vetillard fails to anticipate the claims.

Jensen discloses a micro bioreactor comprising a cell culture chamber bound by two membranes capable of allowing the perfusion of gases, nutrients and water. This is disclosed in Figure 2A and paragraphs [0067]-[0074]. Jensen further teaches in paragraphs [0190] and [0194] that diffusion through the membranes is produced through the transmission of hydrostatic pressure.

Vetillard and Jensen are analogous art because they are from the same field of endeavor regarding bioreactors comprising gas permeable membranes.

At the time of the invention, it would have been obvious to ensure that the Vetillard apparatus allows for the transmission of a hydrostatic pressure capable of promoting diffusion of desired compounds through the membranes. As evidenced by

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Jensen, hydrostatic pressure within the culture and fluid chambers can be precisely controlled in order to promote appropriate culture conditions. One of ordinary skill would have recognized that only minor (if any) structural alterations would be necessary to generate a hydrostatic pressure within the apparatus of Vetillard.

With respect to claim 10, Vetillard discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly indicate that the membrane is optically transparent.

Jensen discloses a bioreactor comprising a plurality of chambers divided by a plurality of membranes (see Figure 2A). Jensen teaches that the gas permeable membranes are constructed from optically transparent materials. This is described throughout the reference and is presented in claim 19.

Vetillard and Jensen are analogous art because they are from the same field of endeavor regarding bioreactors comprising gas permeable membranes.

At the time of the invention, it would have been obvious to ensure that the membranes disclosed by Vetillard are constructed from optically transparent materials. Jensen teaches that this is beneficial because it allows one to better detect cell growth and metabolism using sensors that rely on bioluminescence. As evidenced by Jensen, biocompatible optically transparent membrane materials are readily available in the art.

With respect to claim 11, Vetillard and Jensen disclose the apparatus set forth in claim 10 as set forth in the 35 U.S.C. 103 rejection above. In addition, Jensen teaches

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in paragraph [0103] that the interior surfaces of the bioreactor are coated with a material resistant to cell attachment. Claims 28 and 29 further disclose the use of a substance that decreases adsorption of cells.

At the time of the invention, it would have been obvious to ensure that the gas permeable membrane disclosed by Vetillard was coated by a material resistant to cell attachment. One of ordinary skill in the art would have found it desirable to prevent attachment of cells to the Vetillard membrane in order to avoid clogging of the membrane pores. As evidenced by Jensen, coatings that decrease adsorption of cells to a surface are known in the art.

With respect to claim 13, Vetillard discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejection above. In addition, Jensen states in paragraphs [0161] and [0176] that magnetic stir bars are used to agitate the cell solution during fermentation.

At the time of the invention, it would have been obvious to use the magnetic impellers disclosed by Jensen in the first liquid medium chamber disclosed by Vetillard. Jensen teaches that magnetic stir bars are well known in the art, simple in operation, and effective in agitating and aerating a solution.

With respect to claim 42, Vetillard discloses the apparatus set forth in claim 1, however does not expressly state that the gas permeable membranes are identical.

Jensen discloses the apparatus as previously described above. Jensen additionally teaches in paragraph [0064] that the first and second membranes formed on either side of the culture chamber may be made from the same materials having the same gas diffusivity and solubility properties.

At the time of the invention, it would have been obvious to ensure that the Vetillard membranes were identical. Jensen indicates in paragraph [0064] that it is known in the art to provide membrane pairs that are either identical or different depending on the requirements of the particular cell culture system at hand. More specifically, Jensen indicates that it is known to construct membranes that are specific to the type of culture medium space and/or gas space with which they interact. Accordingly, one of ordinary skill in the art would have recognized that it would have been beneficial to ensure that the Vetillard membranes were identical if both of the membranes interact with the same type of culture fluid or are intended to perform the same function.

Response to Arguments

Applicant's arguments filed 18 May 2010 with respect to the 35 U.S.C. 102 rejections involving Vetillard have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) The recitation in claim 1 that a hydrostatic loading module transmits hydrostatic pressure through a membrane is a functional limitation and not a recitation of intended use.

In response, please consider the following remarks.

Most, if not all, intended use recitations are functional limitations in that they describe how a positively recited element is operated. A limitation does not cease to be an intended use recitation simply because it is deemed to be "functional." While intended use recitations and other types of functional language cannot be entirely disregarded, in apparatus claims intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey*, 370 F.2d 576 (CCPA 1967); *In re Otto*, 312 F.2d 937 (CCPA 1963). Claims directed to apparatus must be distinguished from the prior art in terms of structure rather than function. *In re Danyl*, 263 F.2d 844 (CCPA 1959). See also MPEP 2114. The manner of operating the device does not differentiate an apparatus claim from the prior art. A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitation of the claim. *Ex parte Masham*, 2 USPQ 2d 1647 (BPAI 1987).

The instant case is very similar to *In re Schreiber* cited by Applicant. In that case, the prior art dispensing cap anticipated the claim because it was determined to be fully capable of delivering popcorn, even though the prior art dispensing cap was actually designed for dispensing oil. In the instant case, the Vetillard apparatus is fully capable of imparting a hydrostatic pressure on cell culture chamber by closing fluid

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outlets valve to seal the fluid chambers surrounding the cell culture chamber. Although Vetillard describes one mode of operation, it is fully capable of being used according to a different mode of operation.

(b) Vetillard does not teach or suggest the subject matter recited in claim 1.

In response, please consider the following remarks.

As previously described, Vetillard expressly discloses all of the structural limitations set forth in independent claim 1. Vetillard expressly discloses a module capable of being pressurized to impart a hydrostatic pressure on the adjacent membrane of the cell culture chamber

(c) Structural similarities between Vetillard and illustrated embodiments of the present invention are irrelevant in assessing whether Vetillard anticipates claim 1.

In response, please consider the following remarks.

While not dispositive, it is often useful to compare Applicant's disclosure with the prior art in order to determine whether the prior art device is capable of satisfying the intended use set forth in the claims. In the instant case, Applicant's disclosed bioreactor is almost identical in structure to the bioreactor of Vetillard. This supports the conclusion that the Vetillard pumps, valves, and flow lines may be operated in order to produce hydrostatic pressures within the upper C1 and lower C3 loading modules.

Applicant's arguments filed 18 May 2010 with respect to the 35 U.S.C. 103 rejections involving Vetillard and Jensen have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) The bioreactor of Vetillard is specifically configured and designed to promote fluid circulation using hydrodynamic pressure. Dramatic changes in the Vetillard principle of operation would be necessary in order to promote fluid flow based on hydrostatic pressure.

In response, please consider the following remarks.

It is well within the purview of one of ordinary skill to use known, common and predictable solutions when attempting to arrive at a desired result. In Vetillard, the desired result is the diffusion of critical gases, nutrients and wastes across first and second membranes. Although Vetillard describes the use of a hydrodynamic regime, Jensen indicates that a similar result can be achieved using a hydrostatic regime. While these modes of operation are characterized by slightly different advantages and disadvantages, they are, according to Jensen, largely functionally equivalent in that they produce predictable and effective cell culture conditions. By changing the operation (and not the structure and/or arrangement) of the Vetillard pumps, valves, and flow lines, one of ordinary skill would have been able to controllably and predictably create hydrodynamic forces capable of distributing gases and nutrients to cells in the culture chamber.

(b) It would not have been obvious to redesign the Vetillard apparatus with two membranes having substantially identical gas permeability. Based on the teachings of Vetillard, the membranes have different cutting thresholds and cannot perform the same function.

In response, please consider the following remarks.

While it is agreed that the membranes of the Vetillard apparatus are characterized by different cutting thresholds, Vetillard teaches that this serves to allow the selective diffusion of large molecules such as nutrients, proteins and wastes. There is no evidence that these membranes of Vetillard are characterized by different permeabilities with respect to gases.

Furthermore, one of ordinary skill would have found it obvious to alter and experiment with the particular pore sizes disclosed by Vetillard. It is well known that various cell cultures have different requirements and purposes. For example, in bioreactors where nutrient delivery is paramount, one of ordinary skill would have found it obvious to diffuse nutrients through both membranes of the Vetillard apparatus. The fundamental mode of operation disclosed by Vetillard – the delivery and withdrawal of certain particulates to and from the cell culture – could readily be accomplished using a wide variety of membrane combinations.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN A. BOWERS whose telephone number is (571)272-8613. The examiner can normally be reached on Monday-Friday 7 AM to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nathan A Bowers/
Examiner, Art Unit 1797